CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3257976

Available online at: http://www.iajps.com Research Article

PREPARATION AND CHARACTERIZATION OF POLYMERIC NANOPARTICULATE SYSTEMS CONTAINING ACARBOSE

Krishnamurthy B*[1], Yogananda R[1], Bharathi D. R[2].
[1]PG Department of Pharmaceutics
SJM College of Pharmacy" SJM Campus Chitradurga, Karnataka, India
[2]PG Department of Pharmacology
SJM College of Pharmacy" SJM Campus Chitradurga, Karnataka, India

Article Received: April 2019 **Accepted:** May 2019 **Published:** June 2019

Abstract:
The present study describes formulation and evaluation of nanoparticulate systems containing Acarbose by using synthetic polymers Eudragit RS 100 and eudragit RSPO for the treatment of type 2 Diabetes mellitus. The prepared Nanoparticles were evaluated for Surface morphology, Drug entrapment efficiency, differential scanning colorimetry, particle size, fourier transform infrared spectroscopy, in-vitro drug release and X-ray diffraction studies. The prepared Nanoparticles are smooth in surface and showing spherical shape. The average particle size of the nanoparticles were found in the range of 523 nm to 901 nm. The drug encapsulation efficiency (EE) of the Acarbose nanoparticles were found in the range of 82.21%to 89.30%. Here the drug encapsulation efficiency of prepared nanoparticles were increased with increase in the concentration of the polymer. The X-ray diffractogram of Acarbose has shown characteristic intense peak between the 2Ɵ of 19.67 and 30 due to its crystalline nature. Where as in case of drug free Nanoparticles, no intense peaks related to drug. In drug loaded Nanoparticles peaks were noticed between 2Ɵ of 29.67 and 49. The in-vitro drug release data of all the formulations were found to be zero order and shown sustained release over a period of 24 h. The FTIR Spectra's of Nanoparticles formulation are compared with the spectra of pure drug of Acarbose and there is no much deviation in the spectra's and not observed any drug and polymer interactions. The short time stability study of optimized formulation has done and subjected to drug encapsulation efficiency and In-vitro drug release studies, where results shown that there is no significant change in the formulation.

Keywords: *Acarbose, Nanoparticles, Eudragit RS 100, Eudragit RSPO.*

Corresponding author:
Krishnamurthy B,
PG Department of Pharmaceutics
"SJM College of Pharmacy" SJMIT Campus,
NH4, Chitradurga(577502),
Karnataka, India
(krishnakb07@gmail.com)
Mob: 9008167162, 6362609056

QR code

Please cite this article in press Krishnamurthy B et al., ***Preparation And Characterization Of Polymeric Nanoparticulate Systems Containing Acarbose.,*** *Indo Am. J. P. Sci, 2019; 06[06].*

INTRODUCTION:

Drug delivery is a general term that refers to formulation and administration of a pharmacologically active compound for the purpose of providing an efficient drug plasma concentration, as well as bringing the drug to the specific site of action. Now a day's conventional dosage forms of drugs are rapidly being replaced by the new and the novel drug delivery systems. Amongst, these the controlled release/sustained release dosage forms have become extremely popular in modern therapeutics. The field of nanotechnology has been undergoing tremendous development in the recent decade in pharmacy due to the ability of nanoparticles to interact with complex cellular function and helps to develop multifunctional devices that can target ,diagnose and treat the diseases . Nanotechnology is the ability to work at the atomic, molecular and supra molecular levels (on a scale of ~1-100nm) in order to understand, create and use material structures, devices and systems with fundamentally new properties and functions resulting from their small structure. Diabetes mellitus is a combination of heterogeneous disorders commonly presenting with episodes of hyperglycaemia and glucose intolerance, as a result of lack of insulin, defective insulin action, or both.40 oral hypoglycemic agent such as Acarbose which is a commonly prescribed drug for the treatment of type II diabetes mellitus. It is reported to have a short biological half-life of 2-3 hours and having extremely poor bioavailability of 2 to 5% requiring it to be administered in 2 to 3 divide doses of to 100-250 mg per day.41based on these pharmacokinetic properties we selected this drug as novel targeted drug delivery systems for targeting the diabetes mellitus by the enhancement of bioavailability of the drug.

MATERIALS AND METHODS:

The pure drug Acarbose was obtained as a gift sample from Microlabs Pvt Ltd, Banglore. The polymers Eudragit RSPO and Eudragit RS100 were obtained from Yarrow chemicals and all other chemicals were obtained from SD fine chemicals.

Method of preparation of Acarbose nanoparticles:

Acarbose nanoparticles were prepared by Sonication method by using Probe Sonicator. In this method the Solution of polymer Eudragit RSPO/ Eudragit RS 100 in Chloroform was mixed with 0.3%w/v of polyvinyl alcohol by using controlled flow rate syringe pump (Infusor, Universal Medical Instruments, India) 3ml/min rate. The size of the dropping needle was 0.80 x 38 mm. During this mixing the aqueous phase was sonicated using a probe sonicator set at 10 KHz of energy output (Labman Pro-500) to produce oil in water emulsion. The organic phase was evaporated under reduced pressure. The obtained nanoparticles were recovered by centrifugation (Remi PR 24) at 18000 rpm for 30 min and washed thrice with distilled water. The washing water was removed by a further centrifugation and nanoparticles were freeze dried (Scanvac, Denmark).

Table 01: Formulation table of Acarbose nanoparticles

Formulation	Acarbose(mg)	Eudragit RSPO (w/v)	Eudragit RS 100(w/v)	Chloroform(ml)	Polyvinyl alcohol(w/v)
AC1	100	0.5	-	20	0.3
AC2	100	1	-	20	0.3
AC3	100	1.5	-	20	0.3
AC4	100	2	-	20	0.3
AC5	100	-	0.5	20	0.3
AC6	100	-	1	20	0.3
AC7	100	-	1.5	20	0.3
AC8	100	-	2	20	0.3
AC9	100	1	1	20	0.3

Characterization of Nanoparticles:

Particle size:

Particle size and size distribution are the most important characteristics of nanoparticle systems. They determine the in vivo distribution, biological fate, toxicity and the targeting ability of nanoparticle

systems. In addition, they can also influence the drug loading, drug release and stability of nanoparticles. Here The particle size and distribution is measured by Malvern Zeta sizer by Wet technique. The average particle size of the individual batch of nanoparticles were reported.

Surface morphology:

The surface morphology is also a significant factor in nanoparticle characterization. The surface morphology of a nanoparticle has a huge influence on its performance and properties. The surface morphology is most commonly measured by Scanning Electron microscopy, and Transmission Electron microscopy. Here the surface morphology has been studied by using JEOL JSMT -330A Scanning electron microscopy (SEM).

Zeta potential:

The Zeta potential of a nanoparticle is commonly used to characterize the surface charge property of nanoparticles. It reflects the electrical potential of particles is influenced by the composition of the particle and the medium in which it is dispersed. Nanoparticles with a zeta potential above (±) 30 mV have been shown to be stable in suspension, as the surface charge prevents aggregation of the particles. zeta potential is commonly measured by Malvern zeta analyzer.

FTIR Study:

FTIR spectra of pure drugs and their Eudragit RSPO and RS100 loaded Nanoparticles were recorded on a BRUKER IR spectrophotometer and scanned in the spectral region between 4000 cm−1 and 650 cm−1.

Differential Scanning Colorimetry (DSC):

DSC thermograms of pure drugs and their Eudragit RSPO and RS100 loaded Nanoparticles were recorded on a DSC (TA Instruments, USA, model: SDT 2960). Indium standard was used to calibrate the DSC temperature and enthalpy scale. Nitrogen was used as the purge gas through DSC cell at flow rate of 50 ml per min and 100 ml per min through the cooling unit. The sample (5-10 mg) was heated in a hermetically sealed aluminum pans. Heat runs for each sample were set from 0 to 300° at a heating rate of 10°/min.

Powder X-ray diffraction analysis (PXRD):

PXRD of pure drug and optimized batch of nanoparticles were analysed by Philips PW 1729 X-ray diffractometer. Samples were irradiated with monochromatized Cu Kα-radiations (1.542 A°) and analysed between 2-60° (2θ). The voltage and current used were 30 kV and 30 mA, respectively. The range was 5×103 cycles/s and the chart speed was kept at 100 mm/2θ.

Drug entrapment efficiency:

The nanoparticles were separated from the aqueous medium by ultracentrifugation at 10,000 RPM for 30 min at 50C. Then the resulting supernatant solution was decanted and dispersed into phosphate buffer PH 7.4. Thus the procedure was repeated twice to remove the unentrapped drug molecules completely. The amount of drug entrapped in the nanoparticles was determined as the difference between the total amount of drug used to prepare the Nanoparticles and the amount of drug present in the aqueous medium.

Dissolution Rate study on Nanoparticles:

In-vitro drug release studies were performed in USP Type II dissolution apparatus at rotation speed of 50 rpm. The prepared Nanoparticles were immersed in 900ml of phosphate buffer solution in a vessel, and temperature was maintained at 37±0.20°C. Required quantity 5ml of the medium was withdrawn at specific time periods and the same volume of dissolution medium was replaced in the flask to maintain a constant volume. The withdrawn samples were analyzed using UV spectrophotometer (SHIMADZU 1700).

RESULTS AND DISCUSSION:

Scanning electron microscopic studies (SEM)

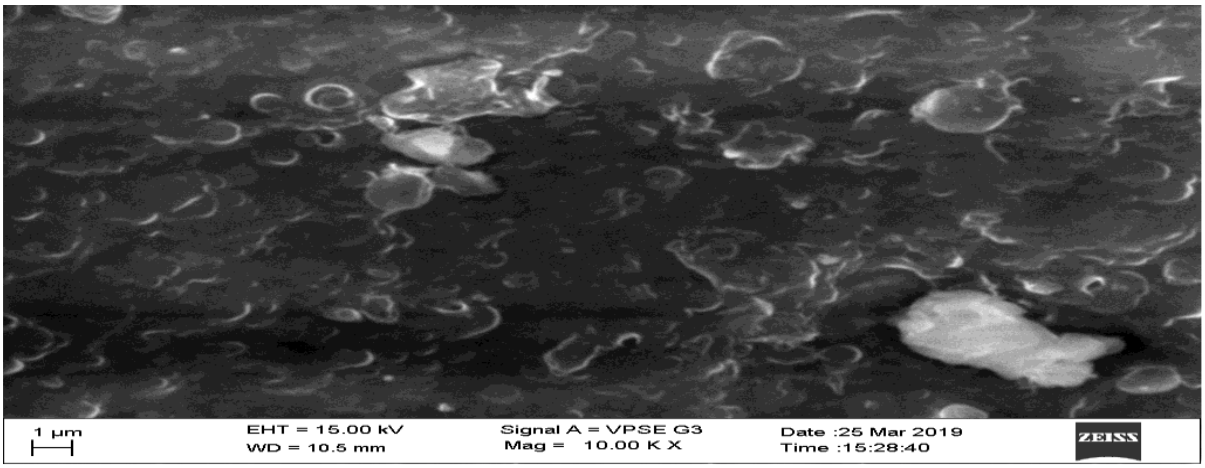
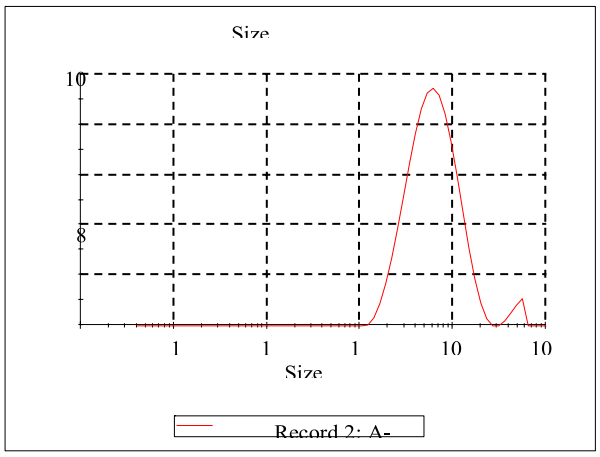


Fig 1:-SEM image of AC9 formulation.

Table 02:- Results of particle size and drug entrapment efficiency

Sl No.	Formulation	Particle size(nm)	Drug EE(%)
01	AC1	536.7	86.57±0.012
02	AC2	682.9	87.91±0.028
03	AC3	724.1	88.17±0.26
04	AC4	670.8	89.30±0.22
05	AC5	813.3	83.02±0.18
06	AC6	798.7	84.56±0.015
07	AC7	568.6	86.23±0.22
08	AC8	901.8	88.62±0.1
09	AC9	523.2	82.21±0.11



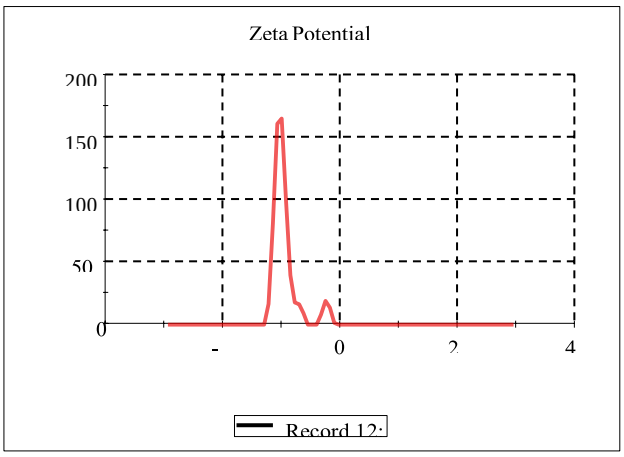


Fig 2 & 3:-Particle size distribution and zeta potential of Acarbose nanoprticles of AC9 formulation

Surface morphology of prepared Nanoparticles was examined by scanning electron microscopic studies (SEM). The SEM photograph showed that the prepared Nanoparticles are having smooth surface and they are spherical in shape. As shown in figure (1). The particles size of the prepared nanoparticles was determined by using particle size analyzer (Malvern) and recorded in the table(01) the average particle size of the Nanoparticles was found in the range of 523 nm to 901 nm and the Zeta potential of the nanoparticles was found to be -16.2 mv hence the formulations are stable. The drug entrapment efficiency (EE) of the Acarbose Nanoparticles were found in the range of 82.21%to 89.30%. Here the drug encapsulation efficiency of prepared Nanoparticles were increased with increase in the concentration of the polymer.

FTIR Studies:

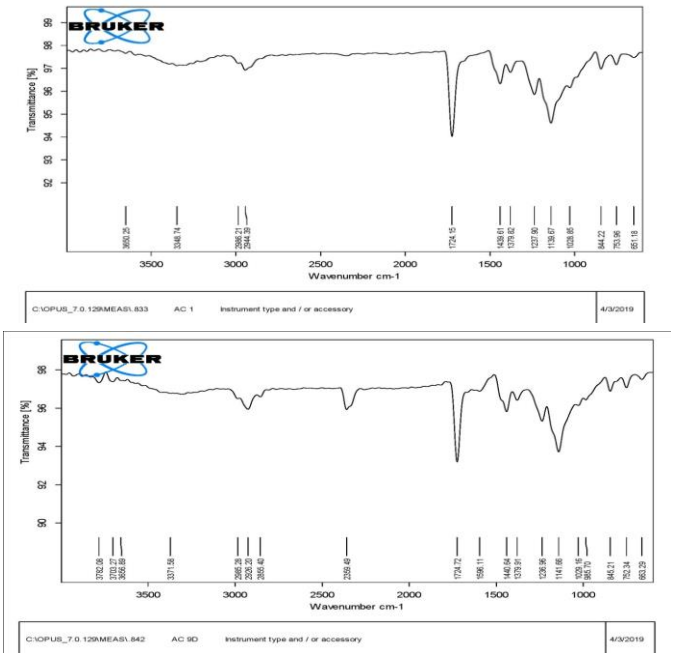


Fig 4& 5: FTIR of Pure Drug and AC9 formulation

The obtained FTIR Spectra's of Nanoparticles formulation are depicted in the figure 4 to 5. Acarbose shows broad peak at 3481.15 cm^{-1} due to OH group and N- H stretching. Large peak was observed at 3061.20 cm^{-1} due to C-H stretching. And shows peak at 2703.27 cm^{-1} due to presence of C=H group, 1641.25 cm^{-1}due to N-H bending, 1401.90 cm^{-1} due to C=C stretching and 1098.26 cm^{-1} due to C-O stretching. Presence of following peaks confirms presence of Acarbose in formulations and the Spectra's of pure drug were compared with the spectra's nanoparticle formulations of Acarbose and there is no much deviation in the spectra's and not observed any drug and polymer interactions.

XRD studies:

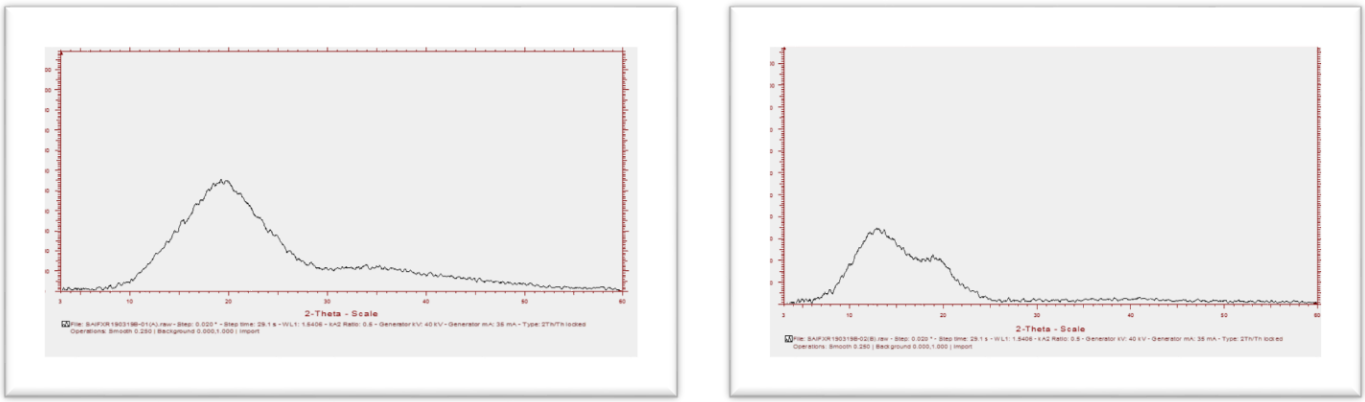
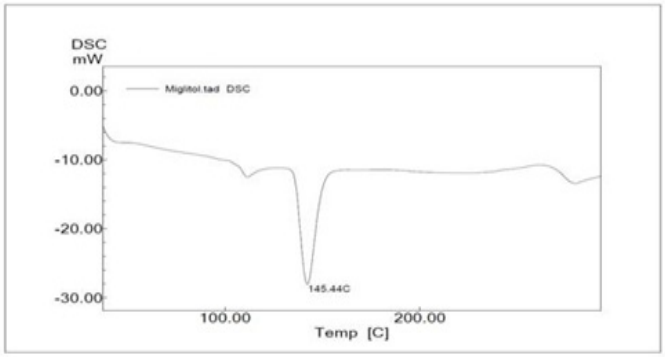


Fig 6&7: XRD graph of pure drug and AC9 formulation

The X-ray diffractograms of pure drug, drug free Nanoparticles and drug loaded Nanoparticles are presented in Fig No (6 to 7). Acarbose has shown characteristic intense peak between the 2Ɵ of 19.67 and 30 due to its crystalline nature. and both the diffractograms drug loaded Nanoparticles and pure drug are identical. This indicates that drug is amorphously dispersed after entrapment in the nanoparticles.

DSC Studies:



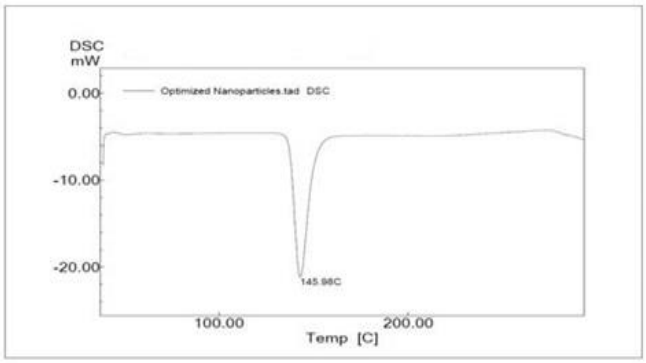


Fig 8 & 9:-DSC spectra of Pure drug & AC9 formulation

The DSC analysis is the most widely used colorimetric technique to characterise the physical state of drug in the formulations. Here the DSC study was carried on pure drug and AC9 formulation and the thermograms are shown in the fig (30&31). Acarbose exhibited a single sharp endothermic peak at 145.44^{0}C due to its glass transition temperature. The optimized formulation has shown sharp endothermic peak 145.98^{0}C. This indicates that the drug was amorphously distributed in the formulations and there is no interaction between the drug and polymer.

Table 03: In-vitro dissolution study of Acarbose nanoparticles

Time (hrs)	% CDR								
	AC1	AC2	AC3	AC4	AC5	AC6	AC7	AC8	AC9
0.5	6 ±0.025	11.35 ±0.028	14.22 ±0.018	3.55 ±0.012	4.12 ±0.015	3.15 ±0.018	3.25 ±0.012	4.25 ±0.025	3.22 ±0.016
1	12 ±0.015	15.52 ±0.017	25.14 ±0.015	10.33 ±0.028	12.45 ±0.026	8.55 ±0.025	10.15 ±0.025	5.69 ±0.032	5.14 ±0.021
1.5	16.76 ±0.031	21.01 ±0.032	29.43 ±0.029	16.15 ±0.031	16.86 ±0.029	18.95 ±0.031	18.12 ± 0.035	17.96 ±0.021	9.43 ±0.025
2	20.12 ±0.011	35.25 ±0.022	33.25 ±0.024	21.25 ±0.014	22.48 ±0.015	35.01 ±0.024	21.02 ±0.024	21.22 ±0.013	10.25 ±0.035
3	36.24 ±0.019	49.36 ±0.015	40.85 ±0.036	32.85 ±0.031	32.1 ±0.012	42.03 ±0.036	32.32 ±0.036	26.58 ±0.025	12.32 ±0.015
4	55.25 ±0.025	65.75 ±0.016	56.6 ±0.015	55.15 ±0.024	58.65 ±0.032	58.05 ±0.012	38.15 ±0.013	33.86 ±0.014	15.22 ±0.014
5	72.16 ±0.031	73.25 ±0.031	72.65 ±0.029	70.35 ±0.031	62.15 ± 0.024	61.08 ±0.021	59.85 ±0.031	37.57 ±0.035	16.75 ±0.024
6	75.82 ±0.011	74.2 ±0.021	74.93 ±0.022	73.76 ±.0.16	64.02 ±0.036	65.42 ±0.029	60.95 ± 0.021	38.25 ±0.017	25.0 ±0.029
7	77.43 ±0.03	74.72 ±0.012	78.32 ±0.017	75.12 ±0.032	65.62 ±0.016	67.26 ±0.025	64.52 ±0.019	44.89 ±0.028	30.15 ±0.028
8	82.91 ±0.027	75.14 ±0.036	79.56 ±0.014	76.55 ±0.025	69.35 ±0.034	72.16 ±0.024	69.25 ±0.017	48.25 ±0.025	33.89 ±0.034
9	86.26 ±0.021	80.45 ±0.031	79.93 ±0.035	76.95 ±0.023	70.14 ±0.019	73.75 ±0.026	73.23 ±0.024	57.68 ±0.034	38.66 ±0.023
10	88.75 ±0.035	82.06 ±0.017	80.06 ±0.027	77.68 ±0.017	76.15 ±0.031	74.15 ±0.021	74.35 ±0.025	63.45 ±0.023	40.15 ±0.028
11	89.22 ±0.031	84.84 ±0.024	81.45 ±0.029	77.95 ±0.012	78.15 ±0.013	74.95 ±0.012	75.22 ±0028	64.45 ±0.028	49.89 ±0.024

12	90.11 ±0.017	86.73 ±0.032	83.67 ±0.018	78.45 ±0.019	79.45 ±0.021	75.16 ±0.018	76.65 ±0.032	65.19 ±0.026	52.22 ±0.021
18	91.33 ±0.013	87.85 ±0.037	86.25 ±0.035	79.25 ±0.029	82.15 ±0.028	78.16 ±0.026	78.56 ±0.034	75.05 ±0.024	68.72 ±0.014
24	92.4 ±0.012	88.18 ±0.021	88.98 ±0.023	80.95 ±0.035	89.95 ±0.019	83.75 ±0.015	79.33 ±0.014	80.05 ±0.019	75.15 ±0.034

The *In-vitro* drug release study was performed using type 2 dissolution test apparatus in P^H 1.2 phosphate buffer and in P^H 7.4 phosphate buffer (Gastric P^H and Intestinal P^H) by using cellophane membrane. the dissolution profile of the Acarbose Nanoparticles are given in the table (6,7,8) and figure (32 to 43) the table shows the in-vitro drug release data for the formulation AC1- AC9 was found to be 92.4%, 88.18%, 88.98%, 80.95%, 89.95%, 83.75%, 79.33%, 80.05% and 75.15% respectively at the end of 24th hour.

Table 04:- Kinetic values of Acarbose Nanoparticles

Formulation code	Zero order Equation		First order		Higuchi model	Peppas Equation	
	N	R^2	N	R^2	R^2	N	R^2
AC1	4.245	0.674	0.055	0.7808	0.846	0.752	0.911
AC2	3.529	0.691	0.035	0.9041	0.875	0.574	0.909
AC3	3.286	0.764	0.033	0.8991	0.922	0.453	0.965
AC4	3.558	0.847	0.029	0.7931	0.952	0.723	0.970
AC5	3.714	0.844	0.033	0.9293	0.966	0.645	0.971
AC6	3.845	0.847	0.027	0.8767	0.957	0.862	0.960
AC7	3.443	0.941	0.028	0.9230	0.979	0.797	0.982
AC8	3.579	0.905	0.024	0.9640	0.976	0.816	0.969
AC9	3.396	0.957	0.020	0.8875	0.961	0.870	0.975

Stability Study Report:

The Prepared Nanoparticles were packed in screw capped HDPE bottles and were stored at 40± 2^0 C and 75 % RH for 45 days. After storage for 45 days, the products were tested for drug entrapment efficiency and drug release study as per the methods described earlier. The results are given in Table

Formulation	Drug entrapment efficiency	
	Before stability test	After stability test
AC9	82.21	82.15

Dissolution Study of optimized Nanoparticle was studied according to earlier procedure and determined drug release rate.

Formulation	Percentage of drug release	
	Before stability test	After stability test
AC9	75.15	74.95

The short term stability study of optimized formulation conducted at 45- 50°C (75%RH) for a period of 45 days to assess Stability as per ICH guidelines. At fixed time, the formulation was evaluated for drug entrapment efficiency and In- vitro drug release study, where results shown that there is no significant change in formulations.

CONCLUSION:

From the results it can be concluded that biocompatible and cost-effective polymer like Eudragit RSPO and Eudragit RS 100 can be used to formulate an efficient Nanoparticles formulation with good percentage entrapment efficiency and practical yield. The particle size analysis indicated that the particles were in the size range of 468.8-536.7 nm, and showed good flow properties. The Nanoparticles were smooth, as shown by the scanning electron microscopic studies. In-vitro drug release showed that release from the Nanoparticles gets successfully retarded for over 24h. The formulations were found to be stable in Short term stability studies. Pharmacokinetic studies indicates that the In-vitro drug release of the formulations fitted Peppas model and the mechanism follows non- Fickian drug release. By considering the results obtained from In-Vitro and Stability studies, it can be suggested that there is further scope for the In-Vivo and the Pharmacokinetic Study. Here we have selected AC9 has a optimized formulation which shown good morphological features, drug entrapment efficiency and controlled drug release.

REFERENCES:

01. Ahmed TA, Aljaeid BM. Preparation, characterization, and potential application of chitosan, chitosan derivatives, and chitosan metal nanoparticles in pharmaceutical drug delivery. Drug design, development and therapy. 2016;10:483-507.
02. Parashar T, Soniya SV, Singh G, Tyagi S, Patel C, Gupta A. Novel oral sustained release technology: a concise review. Int J Res Dev Pharm Life Sci. 2013 Feb; 2(2):262-269.
03. Subramani K, Pathak S, Hosseinkhani H. Recent trends in diabetes treatment using nanotechnology. Digest J of Nanomaterials & Biostructures . 2012 Feb 1;7(1):85-95.
04. Piero MN, Nzaro GM, Njagi JM. Diabetes mellitus-a devastating metabolic disorder. Asian j of biomedical and pharm Sci. 2015 Jan 1;5(40):1-7.
05. Jamzad S, Fassihi R. Development of a controlled release low dose class II drug-Glipizide. Int J of pharmaceutics. 2006 Apr 7;(2):24-32.
06.Kumar G, Juyal V, Badoni PP, Kumar S, Rawat MS. Spectrophotometric Method Development of Acarbose from Bulk and In Its Tablet Dosage Form. J of Pharm Res. 2009 Oct;2(10):1595-1597.
07. Kumar G, Juyal V, Badoni PP. Formulation and evaluation of matrix tablets of acarbose. In vitro. 2010 May; 1:2201-2208.
08.Lokhande AB, Deshmukh TA, Patil VR. Evaluation of repaglinide encapsulated nanoparticles prepared by sonication method. Int J of Pharm and Pharm Sci. 2013;5(3):517-20.
09. Ahmed TA, Aljaeid BM. Preparation, characterization, and potential application of chitosan, chitosan derivatives, and chitosan metal nanoparticles in pharmaceutical drug delivery. Drug design, development and therapy. 2016;10:483-507.
10. Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticle: An overview of preparation and characterization. J of Applied Pharm Sci. 2011 Nov;1(6):228-234.
11. Sáez V, Mason T. Sonoelectrochemical synthesis of nanoparticles. Molecules. 2009;14(10):4284-4299.
12. Subramani K, Pathak S, Hosseinkhani H. Recent trends in diabetes treatment using nanotechnology. Digest J of Nanomaterials & Biostructures (DJNB). 2012 Jan 1;7(1).85-95
13. Sreelola VU, Sailaja AK. Preparation and characterisation of ibuprofen loaded polymeric nanoparticles by solvent evaporation technique. Int J of Pharmacy and Pharm Sci. 2014;6(8):416-421.
14. Abdulhussien M, Aljebory, Tamadhur M,Alsalman. Chitosan Nanoparticles: Review . Imperial J of Interdisciplinary Res.2017;3(7):233-244.
15. Jawahar N, Meyyanathan SN. Polymeric nanoparticles for drug delivery and targeting: A comprehensive review. Int J of Health & Allied Sci. 2012 Oct 1;1(4):217-223.
16. Shubhika K. Nanotechnology and medicine-The upside and the downside. Int. J. Drug Dev. Res. 2012;5(1):1-10.
17. Heera P, Shanmugam S. Nanoparticle characterization and application: an overview. Int. J. Curr. Microbiol. App. Sci. 2015;4(8):379-386.
18. Shelake SS, Patil SV, Patil SS. Formulation and evaluation of fenofibrate-loaded nanoparticles by precipitation method. Indian J of Pharm Sci. 2018 May 31;80(3):420-427.